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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/658,283	09/08/2000	C Alexander Turner Jr	LEX-0041-USA	3550

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EXAMINER	
MURPHY, JOSEPH F	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 08/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/658,283	TURNER JR ET AL.	
	Examiner	Art Unit	
	Joseph F. Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6/13/2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-2 and 6-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 6-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

Claims 1-2, 6-9 are pending and under consideration.

Response to Amendment

Applicant's arguments filed 10/12/2004 have been fully considered but they are persuasive in part.

The rejection of claims 7, 9 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a host cell in culture comprising a polynucleotide with the sequence as set forth in SEQ ID NO: 1, does not reasonably provide enablement for in vivo transfection, has been withdrawn based on Applicant's argument that transgenic animals are limited to non-human primates in the Specification.

The rejection of claims 7, 9 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter, has been withdrawn based on Applicant's argument that transgenic animals are limited to non-human primates in the Specification.

Remaining issues are set forth below

Claim Rejections - 35 USC §§ 101, 112 first paragraph

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 6-9 stand rejected, under 35 U.S.C. § 101 because they are drawn to an invention with no apparent or disclosed patentable utility, for reasons of record set forth the Office action sent 7/1/2002, 12/26/2002, 4/6/2004 and 01/10/2005. The instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose the biological role of this protein or its significance. Applicant is directed to the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday January 5, 2001.

According to MPEP 2107, a rejection for lack of utility is imposed when an invention lacks an asserted specific and substantial utility for the claimed invention and it does not have a readily apparent well-established utility. An invention has a well-established utility if (i) a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties or applications of a product or process), and (ii) the utility is specific, substantial, and credible. In the instant case, the preponderance of the evidence indicates that a person of ordinary skill in the art would not immediately appreciate why the invention is useful based on the characteristics of the invention, for the reasons set forth above, and further, that the claimed invention lacks a specific or substantial utility.

Applicant argues i) that the Specification asserts that SEQ ID NO:2 is a GPCR and that this is sufficient to meet the utility requirement. However, there is insufficient evidence that SEQ ID NO: 2 is a GPCR because the art teaches that it is impossible to predict precisely the functions of protein molecules solely base upon sequence analysis, in view of the diversity of structure and functions of GPCRs (Bork and Eugene V. Koonin, Nature Genetics 18:313-

318,1998). There were nearly 2000 GPCRs up to 1998 and they are classified into over 100 subfamilies according to sequence homology, ligand structure, and receptor function. There are putative seven transmembrane molecules, which do not appear to be coupled to a G protein (Ji et al., J. Biol. Chem. 273:17299-17302, 1998; see beginning of the article). A variety of studies have shown that minor differences in sequence can account for different binding affinities and activities. For example, a change of two-amino acid residues in a protein results in switching the binding of the protein from one receptor to another (Yan et al., Science 290: 523-527, 2000).

ii) However, even assuming, arguendo, that SEQ ID NO: 2 is a GPCR, the ligand is not known, and thus is an orphan GPCR. The previously cited Stadel reference teaches that Stadel et al. teaches that a receptor obtained by bioinformatics technologies is an orphan receptor of unknown function with no apparent relationship to a disease indication (page 434, bridging paragraph, columns 1-2). Stadel et al. further teaches that the initial challenge is to determine the function of each orphan receptor through the identification of activating ligands and, once the function is clarified, link the orphan receptor to a specific disease and thus establish it as a candidate for a comprehensive drug discovery effort (page 433, column 1, first paragraph). Without knowing any further information in regard to function or a relationship to a disease indication, it appears that this starting material provides the barest information in regard to utility. Thus Stadel et al. teaches that before an orphan GPCR has a use, the activating ligand must be determined. Thus, without a known ligand, orphan GPCR receptors do not have a well-established, specific or substantial utility. Since the ligand for SEQ ID NO: 2 is not known, the protein does not have a well-established, specific or substantial utility.

iii) Applicant further argues that evidence submitted after the filing of the instant Application indicates that a knock-put mouse in which the murine ortholog of the nucleic acid encoding SEQ ID NO: 2 was disrupted resulted in death or an increase in blood pressure of the mice. Applicant further argues that the production of a knockout mouse demonstrated that the polynucleotide of SEQ ID NO: 2 encoded a protein which was involved in regulation of systolic blood pressure, and that the polynucleotide would thus have a utility in finding compounds to treat heart disease and abnormal blood pressure. However, there are two problems with this alleged utility. First, the arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). The results of the knock-out mouse experiments are not in the Specification, nor were they presented as a Declaration. Secondly, Applicant must provide evidence that one of ordinary skill in the art would have recognized that the identified specific and substantial utility was well-established at the time of filing. In the instant case, the results of the knock-out mouse experiments are not in the Specification, and thus one of skill in the art would not have recognized the specific and substantial utility at the time of filing.

iv) Applicant further argues that the claimed nucleotide sequence shares 93% percent identity at the amino acid level with a sequence present in GenBank which has been annotated as VIGR GPCR mRNA (GenBank, Accession No. AAO13250). This has been fully considered but is not deemed to be persuasive because (i) the annotation for the published sequence in Genbank is, again, based upon sequence homology and there is no sufficient and credible information that indicates the published sequence is a truly functional GPCR; and (ii) even if the cDNA encodes a functional GPCR, the sequence similarity does not render the sequence of the present invention a

specific function and a patentable utility because there is no single well-established utility for the GPCR family due to the great diversity in structures and functions of the GPCR family and the functions of a GPCR has to be determined experimentally as noted immediately above. Applicant cites the Stehlik reference that teaches that the protein that is 93% identical to SE ID NO: 2 is a member of the adhesion family of GPCRs. According to MPEP 2107, in order for Applicant to rebut the rejection for lack of utility imposed because the invention lacks an asserted specific and substantial utility for the claimed invention and it does not have a readily apparent well-established utility, Applicant must provide evidence that one of ordinary skill in the art would have recognized that the identified specific and substantial utility was well-established at the time of filing. The examiner should also ensure that there is an adequate nexus between the evidence and the properties of the now claimed subject matter as disclosed in the application as filed. That is, the applicant has the burden to establish a probative relation between the submitted evidence and the originally disclosed properties of the claimed invention. In the instant case, the Stehlik reference sets forth that an amino acid sequence 93% identical to SEQ ID NO: 2 is a member of the adhesion family of GPCRs. The publication date of this reference is July, 2004, while the filing date of the instant application is 09/08/2000. Thus, the reference which establishes that VIGR is an adhesion molecule is post-filing, and as such, does not provide evidence that one of ordinary skill in the art would have recognized that the identified specific and substantial utility was well-established at the time of filing. At the time of filing the function of the SEQ ID NO: 2 polypeptide was not known, nor were any specific disease associations known, and this reference does not show that the SEQ ID NO: 2 polypeptide had a well-established utility at the time of filing. Additionally, the Stehlik et al. reference establishes that a

polypeptide 93% identical to SEQ ID NO: 2 polypeptide is an adhesion molecule. In the instant case the Specification is silent with regards to the protein of SEQ ID NO: 2 functioning as an adhesion molecule, thus there is insufficient nexus between the Specification as filed and the teaching of Stehlik et al.

v) Applicant further argues that the facts of the instant case are similar to Example 10 of the utility guidelines. However, in Example 10 of the Revised interim Utility Guidelines Training Materials, the claimed nucleic acid sequence has a well-established utility because the high sequence homology can place the protein encoded by the claimed nucleic acid sequence in a DNA ligase family, whereas ligases have a well-established use in ligating DNA. Here, however, the utility claim is based upon homology to a protein that is only 93% identical to SEQ ID NO: 2, and furthermore, at the time of filing the homology to an adhesion molecule was not disclosed in the Specification, and thus there was not a probative relation between the submitted evidence and the originally disclosed properties of the claimed invention.

Claim 2 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a complement of a nucleic acid which hybridizes to a nucleic acid encoding SEQ ID NO: 2, or a nucleic acid which hybridizes to a complement of a nucleic acid of SEQ ID NO: 1. The claims thus encompass variants of nucleic acids. However, Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible variants of SEQ ID NO: 2. It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function.

Applicant argues that the instant claimed sequences are defined based on the structural features because methods of hybridization can be used to isolate sequences which hybridize under the conditions listed in the claim to the sequence set forth in SEQ ID NO: 1. However, the Specification does not set forth a function for the claimed nucleic acids, while the claims encompass variant nucleic acids. The Specification does not disclose the critical nucleic acid residues necessary to maintain any function. The specification does not disclose the correlation between the structure (sequence) of the encompassed nucleic acids and any function. The nucleic acid sequence determines its structural and functional properties, and predictability of which nucleic acids can be substituted is extremely complex and well outside the realm of routine experimentation, because accurate predictions of a polypeptide's structure from mere sequence data are limited. Since detailed information regarding the structural and functional requirements of the nucleic acids are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims. Therefore it would require undue experimentation by one of skill in the art to make and use the invention as claimed without further guidance from the instant specification.

Claim 2 is rejected, under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The claims are drawn to a complement of a nucleic acid which hybridizes to a nucleic acid encoding SEQ ID NO: 2, or a nucleic acid which hybridizes to a complement of a nucleic acid of SEQ ID NO: 1. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The specification and claims do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to the encoded polypeptide. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted.

Applicant argues that the claimed nucleic acids are distinguished on the basis of structural features, i.e. a sequence and that the claims as presented meet the Written Description standard as set forth in the written description guidelines. However, claims 35, 39, 40, 45, 51 are drawn to nucleic acids which hybridize to a representative sequence. However, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical

properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the genus of nucleic acids. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from other seven transmembrane region compounds are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the nucleic acids encompassed: there is no guidance in the art as to what the defining characteristics of the nucleic acids might be. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus as broadly claimed.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Murphy whose telephone number is (571) 272-0877. The examiner can normally be reached Monday through Friday from 7:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (571) 272-0829.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Joseph F. Murphy, Ph. D.
Primary Examiner
Art Unit 1646
August 1, 2005

JOSEPH MURPHY
PATENT EXAMINER